

**Ultrafast optogenetic control.**

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**Funding Grants:** Bioengineering technology for fast optical control of differentiation and function in stem cells and stem cell progeny

**Public Summary:**

**Scientific Abstract:**

Channelrhodopsins such as channelrhodopsin-2 (ChR2) can drive spiking with millisecond precision in a wide variety of cells, tissues and animal species. However, several properties of this protein have limited the precision of optogenetic control. First, when ChR2 is expressed at high levels, extra spikes (for example, doublets) can occur in response to a single light pulse, with potential implications as doublets may be important for neural coding. Second, many cells cannot follow ChR2-driven spiking above the gamma (approximately 40 Hz) range in sustained trains, preventing temporally stationary optogenetic access to a broad and important neural signaling band. Finally, rapid optically driven spike trains can result in plateau potentials of 10 mV or more, causing incidental upstates with information-processing implications. We designed and validated an engineered opsin gene (ChETA) that addresses all of these limitations (profoundly reducing extra spikes, eliminating plateau potentials and allowing temporally stationary, sustained spike trains up to at least 200 Hz).

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